

This listing of claims replaces all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (canceled)

Claim 2. (currently amended)      A manufactured peptide and pharmaceutically acceptable salts thereof comprising a metal ion-binding domain comprising two or more contiguous amino acids and a biological-function domain specific for one or more melanocortin receptors and a metal ion selected from the group consisting of rhenium and technetium complexed to the metal ion-binding domain, wherein at least a portion of said biological-function domain is co-extensive with at least a portion of the metal ion-binding domain, and wherein said biological-function domain is conformationally constrained upon complexing the metal ion-binding domain with a metal ion, and wherein the peptide or salt thereof is substantially more specific for one or more melanocortin receptors when the metal ion-binding domain is complexed with a metal ion than is the peptide or salt thereof when the metal ion-binding domain is not complexed with a metal ion, wherein the peptide is of the formulas:

R<sub>1</sub> – Lll – Aaa – Bbb – Ccc – R<sub>2</sub>,

\_\_\_\_\_ R<sub>1</sub> – Bbb – Aaa – Ccc – R<sub>2</sub>,

\_\_\_\_\_ R<sub>1</sub> – Ddd – Bbb – Aaa – R<sub>3</sub>,

\_\_\_\_\_ R<sub>4</sub> – Eee – Bbb – Ccc – R<sub>2</sub>,

\_\_\_\_\_ R<sub>1</sub> – Hhh – Aaa – Bbb – Ccc – R<sub>5</sub>, or

\_\_\_\_\_ R<sub>1</sub> – lli – lli – Ccc – Jjj – Kkk – R<sub>2</sub>,

\_\_\_\_\_ wherein

R<sub>1</sub> comprises a functionality that potentiates the intrinsic activity of the remainder of the peptide,

including but not limited to providing an auxiliary or secondary receptor contact;

Aaa is an L- or D-configuration cationic amino acid with a positively charged side chain;

Bbb is an L- or D-configuration amino acid with an aromatic side chain;

Ccc is an amino acid that provides both a nitrogen atom (N), from the alpha amino group, and a sulfur atom (S), from a side chain group, for metal ion complexation;

Lll is a D-configuration amino acid with an aromatic side chain;

R<sub>2</sub> is optionally present, and if present, comprises an amino acid with an aromatic side chain;

Ddd is an amino acid that provides an S, from a side chain group, for metal ion complexation;

R<sub>3</sub> is an amino acid with an aromatic side chain that provides an N for metal ion complexation;

R<sub>4</sub> is a functionality that provides a cationic center;

Eee is an uncharged L- or D-configuration amino acid that provides an N for metal ion complexation;

R<sub>5</sub> is an amide, substituted amide, ester or carboxylate group, or comprises an L- or D-configuration amino acid;

Hhh is an L- or D-configuration cationic amino acid with a positively charged side chain;

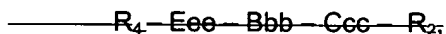
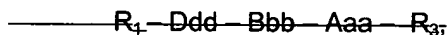
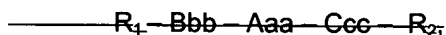
lil is an L- or D-configuration amino acid that provides an N for metal ion complexation;

Jjj is an L- or D-configuration amino acid with an aromatic side chain; and

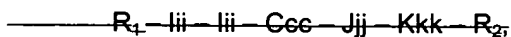
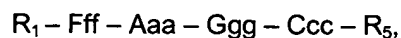
Kkk is an L- or D-configuration cationic amino acid with a positively charged side chain.

Claim 3-17 (Canceled)

Claim 18. (currently amended) ~~The peptide of claim 2~~ A manufactured peptide and pharmaceutically acceptable salts thereof comprising a metal ion-binding domain comprising two or more contiguous amino acids and a biological-function domain specific for one or more melanocortin receptors and a metal ion selected from the group consisting of rhenium and technetium complexed to the metal ion-binding domain, wherein at least a portion of said biological-function domain is co-extensive with at least a portion of the metal ion-binding domain, and wherein said biological-function domain is conformationally constrained upon complexing the metal ion-binding domain with a metal ion, and wherein the peptide or salt thereof is substantially more specific for one or more melanocortin receptors when the metal ion-binding domain is complexed with a metal ion than is the peptide or salt thereof when the metal ion-binding domain is not complexed with a metal ion, wherein the peptide is of the formulas:



of the formula:



wherein

R<sub>1</sub> comprises a functionality that potentiates the intrinsic activity of the remainder of the peptide, including but not limited to providing an auxiliary or secondary receptor contact;

Aaa is an L- or D-configuration cationic amino acid with a positively charged side chain;

~~Bbb is an L- or D-configuration amino acid with an aromatic side chain;~~

Ccc is an amino acid that provides both a nitrogen atom (N), from the alpha amino group, and a sulfur atom (S), from a side chain group, for metal ion complexation;

~~Lll is a D-configuration amino acid with an aromatic side chain;~~

~~R<sub>2</sub> is optionally present, and if present, comprises an amino acid with an aromatic side chain;~~

~~Ddd is an amino acid that provides an S, from a side chain group, for metal ion complexation;~~

~~R<sub>3</sub> is an amino acid with an aromatic side chain that provides an N for metal ion complexation;~~

~~R<sub>4</sub> is a functionality that provides a cationic center;~~

~~Eee is an uncharged L- or D-configuration amino acid that provides an N for metal ion complexation;~~

Fff is an L- or D-configuration aromatic amino acid wherein the aromatic ring of the aromatic side chain of Fff is substituted with halogen, alkyl or aryl groups or is a D-configuration Phe, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl), Tyr(BzlCl<sub>2</sub>), Tic, Tiq or Tca, or derivative, analog or homolog thereof;

Ggg is an L- or D-configuration aromatic amino acid; and

R<sub>5</sub> is an amide, substituted amide, ester or carboxylate group, or comprises an L- or D-configuration amino acid;

~~Hhh is an L- or D-configuration cationic amino acid with a positively charged side chain;~~

~~lil is an L- or D-configuration amino acid that provides an N for metal ion complexation;~~

~~Jjj is an L- or D-configuration amino acid with an aromatic side chain; and~~

~~Kkk is an L- or D-configuration cationic amino acid with a positively charged side chain.~~

Claim 19 - 25. (canceled)

Claim 26. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>1</sub> comprises an amino acid chain of from one to about four neutral or charged L- or D-configuration amino acid residues.

Claim 27. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>1</sub> comprises a linear or branched alkyl, aryl, alkene, alkenyl, or aralkyl chain.

Claim 28. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Aaa is an L-configuration Lys, Arg, Orn, Dpr or Dbu, or derivative, analog or homolog thereof.

Claim 29. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Aaa provides an N for metal ion complexation.

Claim 30. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Bbb is a D-configuration Phe, Phe(4'-Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl), or Tyr(BzlCl<sub>2</sub>), or derivative, analog or homolog thereof.

Claim 31. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the aromatic ring of the aromatic side chain of Bbb is substituted with one or more halogen, alkyl or aryl groups.

Claim 32. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Bbb provides an N for metal ion complexation.

Claim 33. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Ccc is an L- or D-configuration Cys, Pen or Hcys.

Claim 34. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Lll is a D-configuration

Phe, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl), or Tyr(BzlCl<sub>2</sub>), or derivative, analog or homolog thereof.

Claim 35. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the aromatic ring of the aromatic side chain of LII is substituted with one or more halogen, alkyl, or aryl groups.

Claim 36. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein LII does not provide an N for metal ion complexation.

Claim 37. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>2</sub> is an L- or D-configuration Phe, Trp, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>), or derivative, analog or homolog thereof.

Claim 38. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the C-terminus of R<sub>2</sub> is amidated.

Claim 39. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>2</sub> is a des-carboxyl amino acid corresponding to an L- or D-configuration Phe, Trp, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>) .

Claim 40. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>2</sub> is absent.

Claim 41. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Ddd is an L- or D-configuration Cys, Pen or Hcys.

Claim 42. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>3</sub> is an L- or D-configuration Phe, Trp, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe,

Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>), or derivative, analog or homolog thereof.

Claim 43. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the C-terminus of R<sub>3</sub> is amidated.

Claim 44. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>3</sub> is a des-carboxyl amino acid corresponding to an L- or D-configuration Phe, Trp, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>) ~~any of the L- or D-amino acid residues of claim 42.~~

Claim 45. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>4</sub> is an L- or D-configuration Lys, Arg, Orn, Dpr or Dbu, or derivative, analog or homolog thereof.

Claim 46. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the N-terminus of R<sub>4</sub> is functionalized with a neutral amino acid or non-peptide group comprising a linear or branched alkyl, aryl, alkene, alkenyl or aralkyl chain.

Claim 47. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Eee is ~~[[an]]~~ a Gly or an L-configuration Ala, Nle, Leu, Val, Phe or Trp, or derivative, analog or homolog thereof.

Claim 48. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Eee is an amino acid with an aliphatic side chain.

Claims 49 - 50 (canceled)

Claim 51. (previously presented) The peptide of claim 18 wherein Fff does not provide an N for metal ion complexation.

Claim 52. (previously presented) The peptide of claim 18 wherein Ggg is an L-configuration Phe, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal,

Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>), and derivatives, analogs or homologs thereof, including both natural and synthetic amino acids.

Claim 53. (previously presented) The peptide of claim 18 wherein the aromatic ring of the aromatic side chain of Ggg may be substituted with halogen, alkyl or aryl groups.

Claim 54. (previously presented) The peptide of claim 18 wherein Ggg provides an N for metal ion complexation.

Claim 55. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein R<sub>5</sub> is an L- or D-configuration aromatic, aliphatic, neutral or charged amino acid, optionally further comprising an amide group.

Claim 56. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Hhh is an L-configuration Lys, Arg, Orn, Dpr or Dbu, and derivatives, analogs or homologs thereof, including both natural and synthetic amino acids.

Claim 57. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Hhh does not provide an N for metal ion complexation.

Claim 58. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein lli is an Ala, Gly, Nle, Val, Leu, Ile, His, Lys, or Arg, and derivatives, analogs or homologs thereof, including both natural and synthetic amino acids.

Claim 59. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Jjj is a D-configuration Phe, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl), or Tyr(BzlCl<sub>2</sub>), and derivatives, analogs or homologs thereof.

Claim 60. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein the aromatic ring of the aromatic side chain of Jjj is substituted with one or more halogen, alkyl or aryl groups.



Claim 61. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Jjj does not provide an N for metal ion complexation.

Claim 62. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Kkk is an L-configuration Lys, Arg, Orn, Dpr or Dbu, or derivative, analog or homolog thereof.

Claim 63. (currently amended) The peptide of ~~claim 18~~ claim 2 wherein Kkk does not provide an N for metal ion complexation.

Claim 64. (new) The peptide of claim 18 wherein R<sub>1</sub> comprises an amino acid chain of from one to about four neutral or charged L- or D-configuration amino acid residues.

Claim 65. (new) The peptide of claim 18 wherein R<sub>1</sub> comprises a linear or branched alkyl, aryl, alkene, alkenyl, or aralkyl chain.

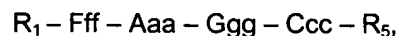
Claim 66. (new) The peptide of claim 18 wherein Aaa is an L-configuration Lys, Arg, Orn, Dpr or Dbu, or derivative, analog or homolog thereof.

Claim 67. (new) The peptide of claim 18 wherein Aaa provides an N for metal ion complexation.

Claim 68. (new) The peptide of claim 18 wherein Ccc is an L- or D-configuration Cys, Pen or Hcys.

Claim 69. (new) A manufactured peptide and pharmaceutically acceptable salts thereof comprising a metal ion-binding domain comprising two or more contiguous amino acids and a biological-function domain specific for one or more melanocortin receptors and a metal ion selected from the group consisting of rhenium and technetium complexed to the metal ion-binding domain, wherein at least a portion of said biological-function domain is co-extensive with at least a portion of the metal ion-binding domain, and wherein said biological-function domain is conformationally constrained upon complexing the metal ion-binding domain with a metal ion, and wherein the peptide or salt thereof is substantially more specific for one or more melanocortin receptors when the metal ion-binding domain is complexed with a

metal ion than is the peptide or salt thereof when the metal ion-binding domain is not complexed with a metal ion, wherein the peptide is of the formula:



wherein

$R_1$  comprises a functionality that potentiates the intrinsic activity of the remainder of the peptide, including but not limited to providing an auxiliary or secondary receptor contact;

Aaa is an L- or D-configuration cationic amino acid with a positively charged side chain;

Ccc is an amino acid that provides both a nitrogen atom (N), from the alpha amino group, and a sulfur atom (S), from a side chain group, for metal ion complexation;

Fff is an L- or D-configuration aromatic amino acid;

Ggg is an L- or D-configuration aromatic amino acid wherein the aromatic ring of the aromatic side chain of Ggg is substituted with halogen, alkyl or aryl groups or is an L-configuration Phe, Phe(4'Cl), Phe(3',4' Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, -Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl) or Tyr(BzlCl<sub>2</sub>), and derivatives, analogs or homologs thereof, including both natural and synthetic amino acids; and

$R_5$  is an amide, substituted amide, ester or carboxylate group, or comprises an L- or D-configuration amino acid.

Claim 70. (new) The peptide of claim 69 wherein Ggg provides an N for metal ion complexation.

Claim 71. (new) The peptide of claim 69 wherein  $R_1$  comprises an amino acid chain of from one to about four neutral or charged L- or D-configuration amino acid residues.

Claim 72. (new) The peptide of claim 69 wherein  $R_1$  comprises a linear or branched alkyl, aryl, alkene, alkenyl, or aralkyl chain.

Claim 73. (new) The peptide of claim 69 wherein Aaa is an L-configuration Lys, Arg, Orn, Dpr or Dbu, or derivative, analog or homolog thereof.

Claim 74. (new) The peptide of claim 69 wherein Aaa provides an N for metal ion complexation.

Claim 75. (new) The peptide of claim 69 wherein Ccc is an L- or D-configuration Cys, Pen or Hcys.

Claim 76. (new) The peptide of claim 69 wherein Fff is a D-configuration Phe, Phe(4'Cl), Phe(3',4'Di-Cl), Phe(4'-nitro), Phe(4'-methyl), Phe(4'-Phenyl), Hphe, Pgl, Trp, 1-Nal, 2-Nal, Ser(Bzl), Lys(Z), Lys(Z-2'Br), Lys(Bz), Thr(Bzl), Cys(Bzl), Tyr(BzlCl<sub>2</sub>), Tic, Tiq or Tca, or derivative, analog or homolog thereof.

Claim 77. (new) The peptide of claim 69 wherein the aromatic ring of the aromatic side chain of Fff is substituted with halogen, alkyl or aryl groups.

Claim 78. (new) The peptide of claim 69 wherein Fff does not provide an N for metal ion complexation.

Claim 79. (new) The peptide of claim 69 wherein R<sub>5</sub> is an L- or D-configuration aromatic, aliphatic, neutral or charged amino acid, optionally further comprising an amide group.